HISTORY OF THE "MADISON" AEROSOL CHAMBER

1968 "First generation" chamber designed by Don Smith, Ernie Wiegeshaus and D. McMurray and built at the UW Machine Shop

Purpose: to deposit small numbers of single bacilli into the alveolar spaces of the lung in a reproducible manner

1970 First publication describing the chamber and its application to TB in guinea pigs

Wiegeshaus EH, et al. Am Rev Resp Dis 102: 422 (1970)

HISTORY OF THE "MADISON" AEROSOL CHAMBER

1983 "Second generation" chamber built at UW Machine Shop and shipped to D. McMurray at Texas A&M University

NIH grants & contracts≈$6 million

>50 grad students, research scientists,post-docs,technicians

>1500 person-hours of contact

Not a single accidental exposure

HISTORY OF THE "MADISON" AEROSOL CHAMBER

1990-2003 More than ten (10) "third generation" chambers built in Madison and installed in laboratories around the world

Design improvements:

1) Construction materials
2) Integrated electronic controls
3) Vacuum guage/fail-safe shutdown
4) Collisson nebulizer
5) Improved animal basket design/loading
6) Integrated air compressor

MADISON AEROSOL CHAMBERS IN USE AROUND THE WORLD

Astra-Zeneca, Bangalore, India

AgResearch Wallaceville, Upper Hutt, NZ

Vet Sciences Div, Belfast, N Ireland

Harvard University, Boston, MA

Rockefeller University, New York, NY

Univ of North Carolina, Chapel Hill, NC

Colorado State Univ, Fort Collins, CO

UT Health Science Ctr, San Antonio, TX

UT Medical Branch, Galveston, TX

Texas A&M Univ HSC, College Station, TX

CURRENT APPLICATIONS OF THE MADISON AEROSOL CHAMBER TO INFECTIOUS DISEASE RESEARCH

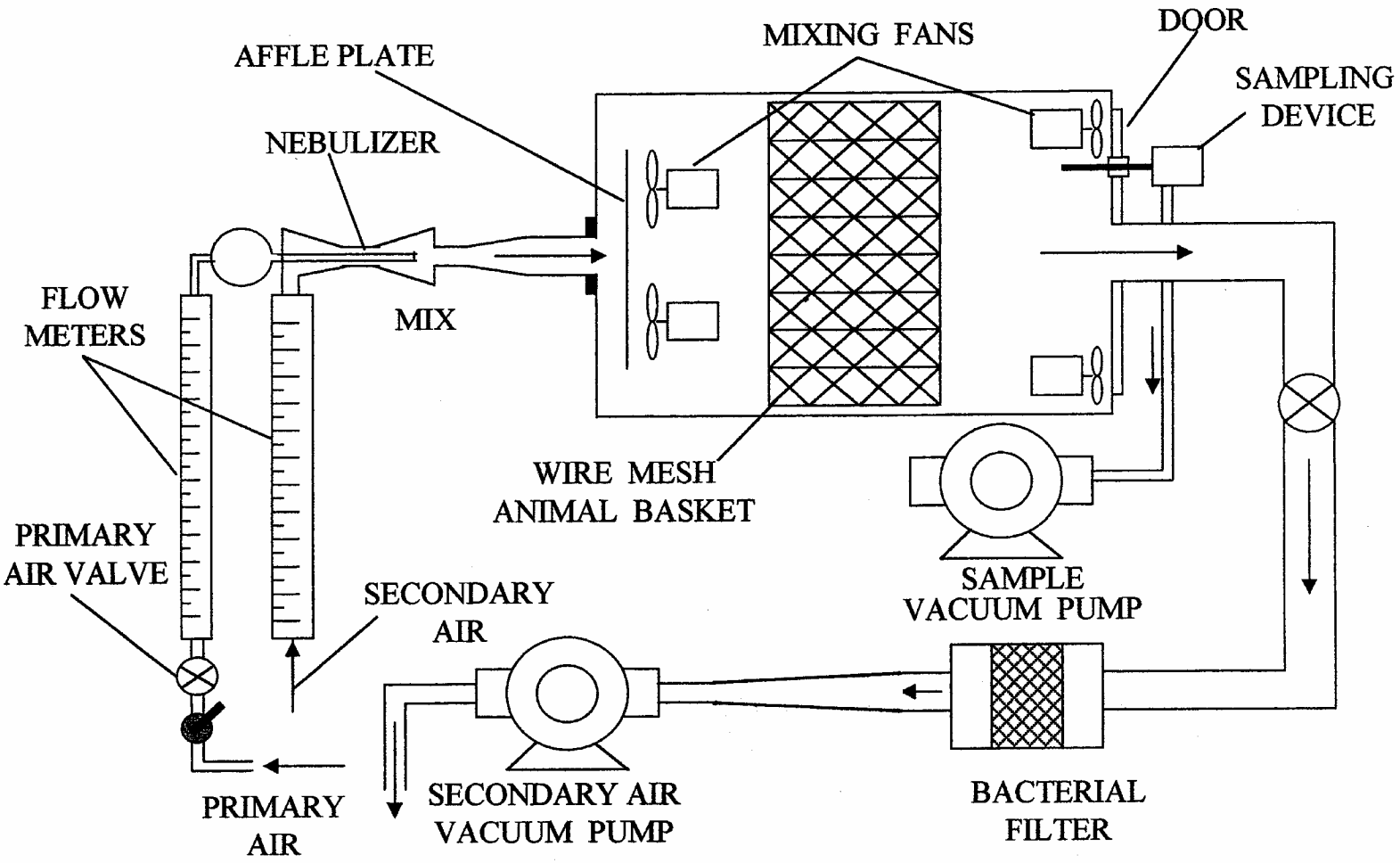
I. Pathogens

Mycobacterium tuberculosis
Mycobacterium bovis
Other mycobacteria
Coxiella burnetii
Aspergillus spp
Francisella
Brucella spp
Bacillus anthracis
Coccidiodes immitus

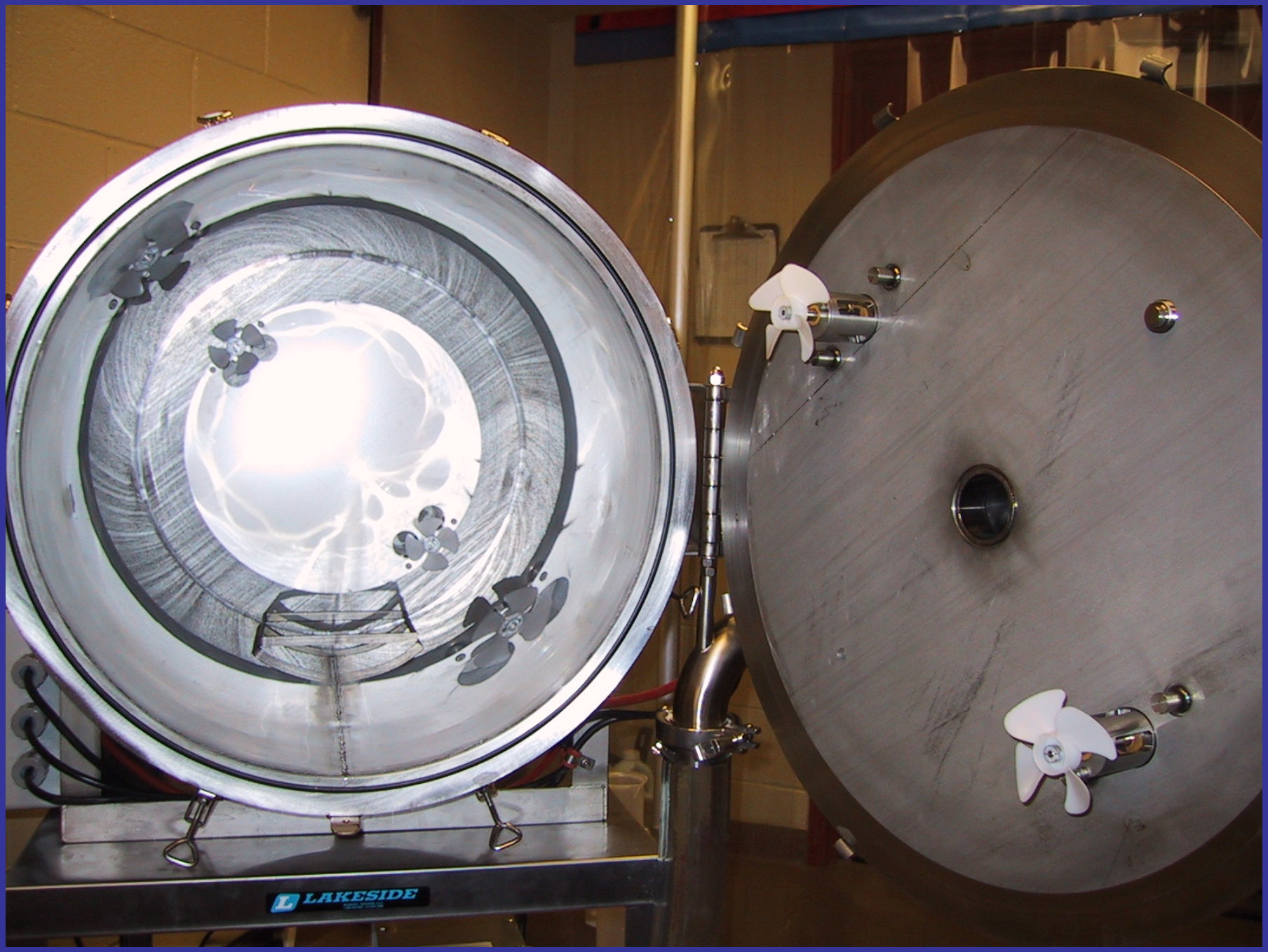
II. Experimental hosts

Guinea pigs
Mice
Hamsters
Rabbits
Brush-tail possums
Heifers

Schematic diagram of the components of the aerosol infection chamber




FANS
NEBULIZER
TEST
TEST
POWER
END CYCLE


LAKESIDE


FANS
NEBULIZER
START
TEST
TEST
POWER
END CYCLE
INCHES OF WATER
0
10
20
30
40
50
PHOTOHELIC
Dwyer
ZERO
EMERGENCY STOP
RESET

SAFETY FEATURES OF THE MADISON AEROSOL CHAMBER

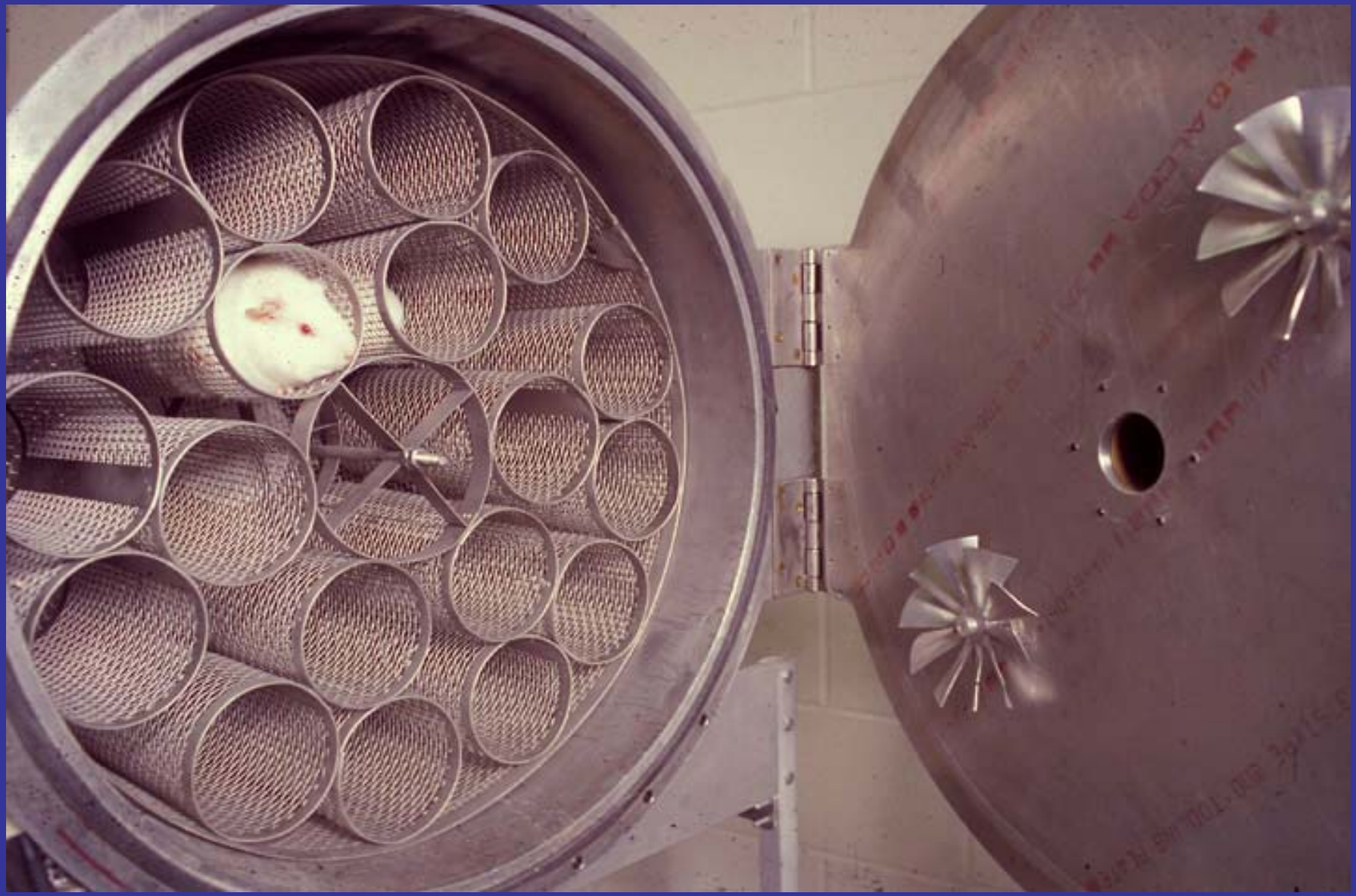
1) Entire system sealed and under negative pressure
   a. Vacuum pump operates continuously
   b. Vacuum is quantified
   c. Loss of vacuum triggers shutdown of nebulizer

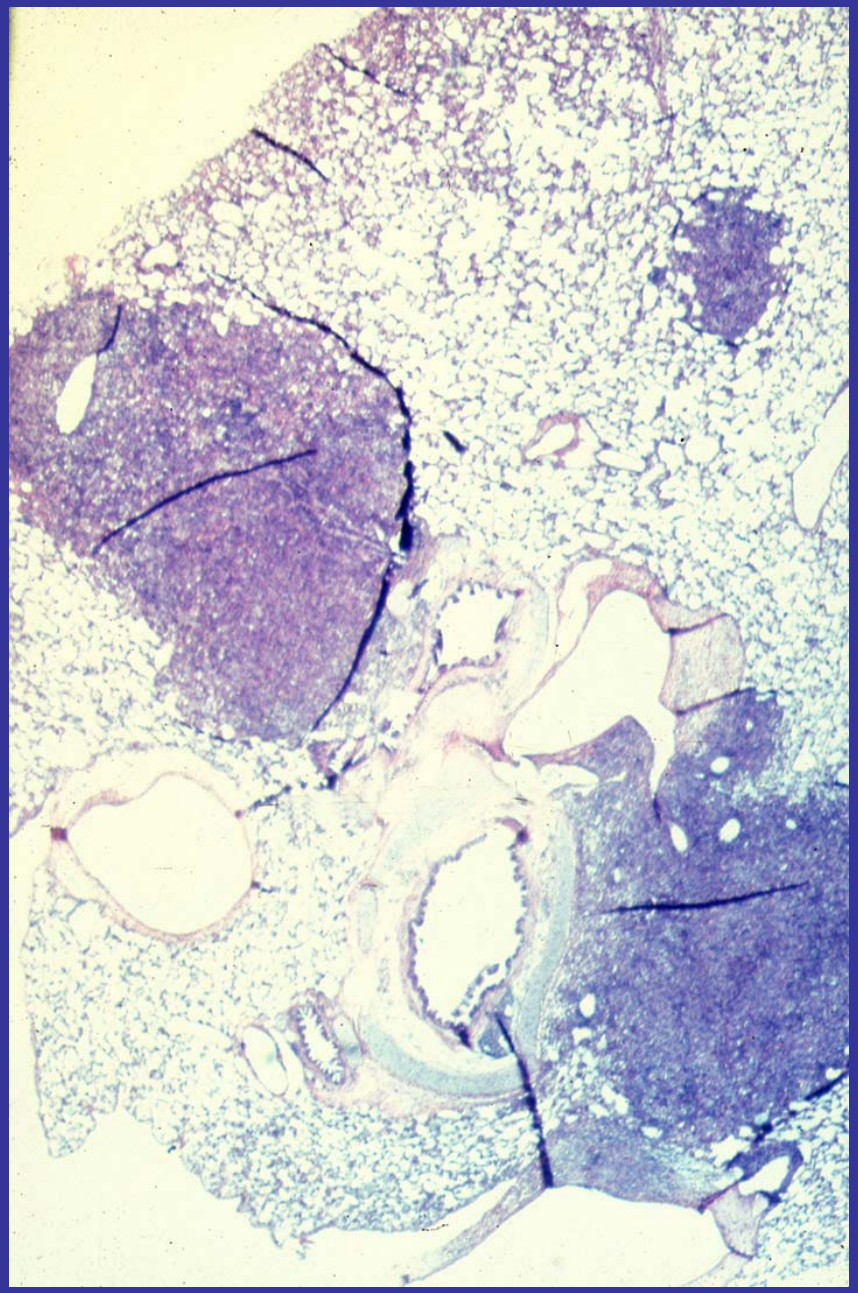
2) Very high proportion of respirable particles (droplet nuclei) requires very low concentration of bacilli in the air (<400 cfu/liter)

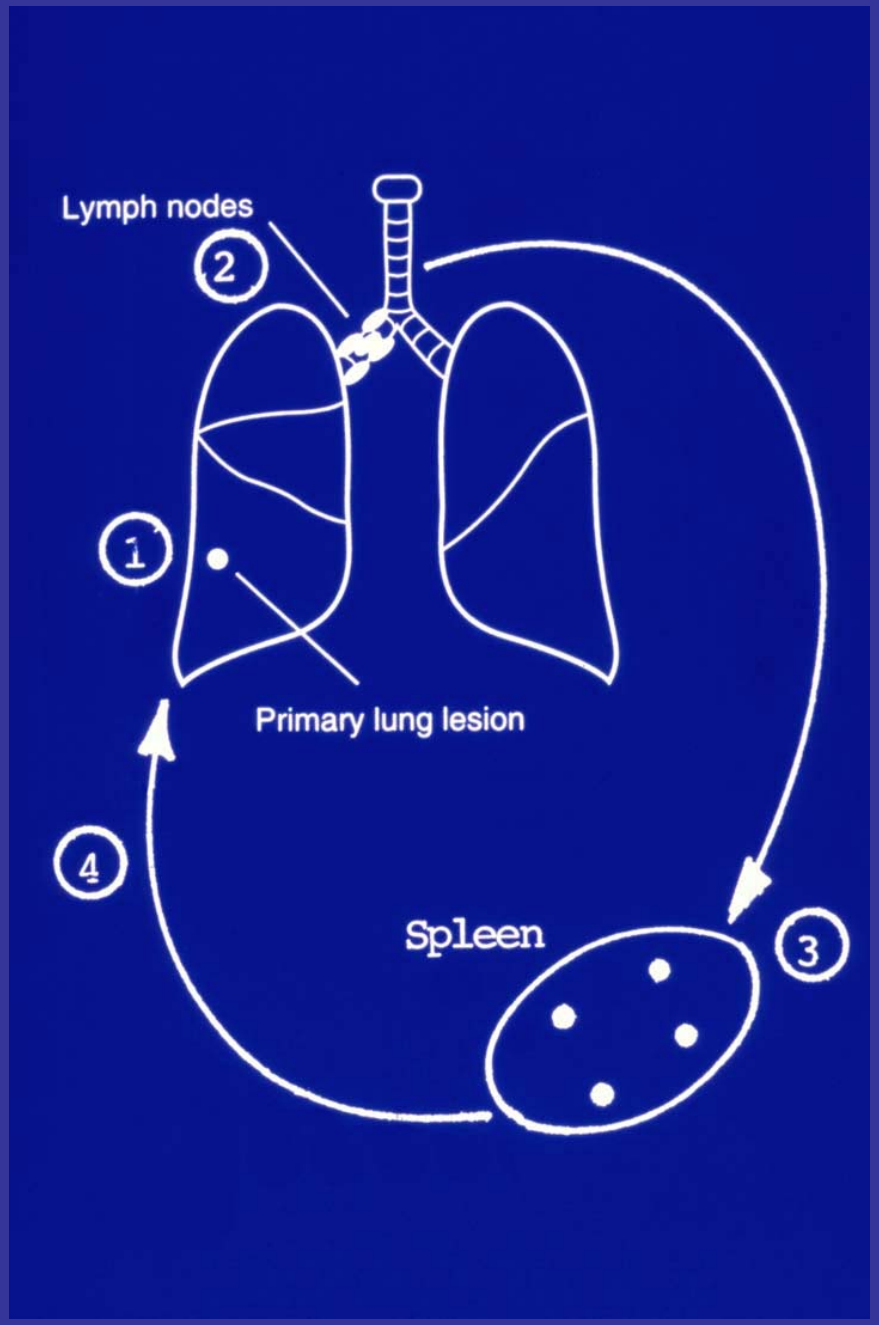
3) Long washout period with fresh room air (10 min @ 50 liters/min) ensures removal of essentially all airborne bacilli

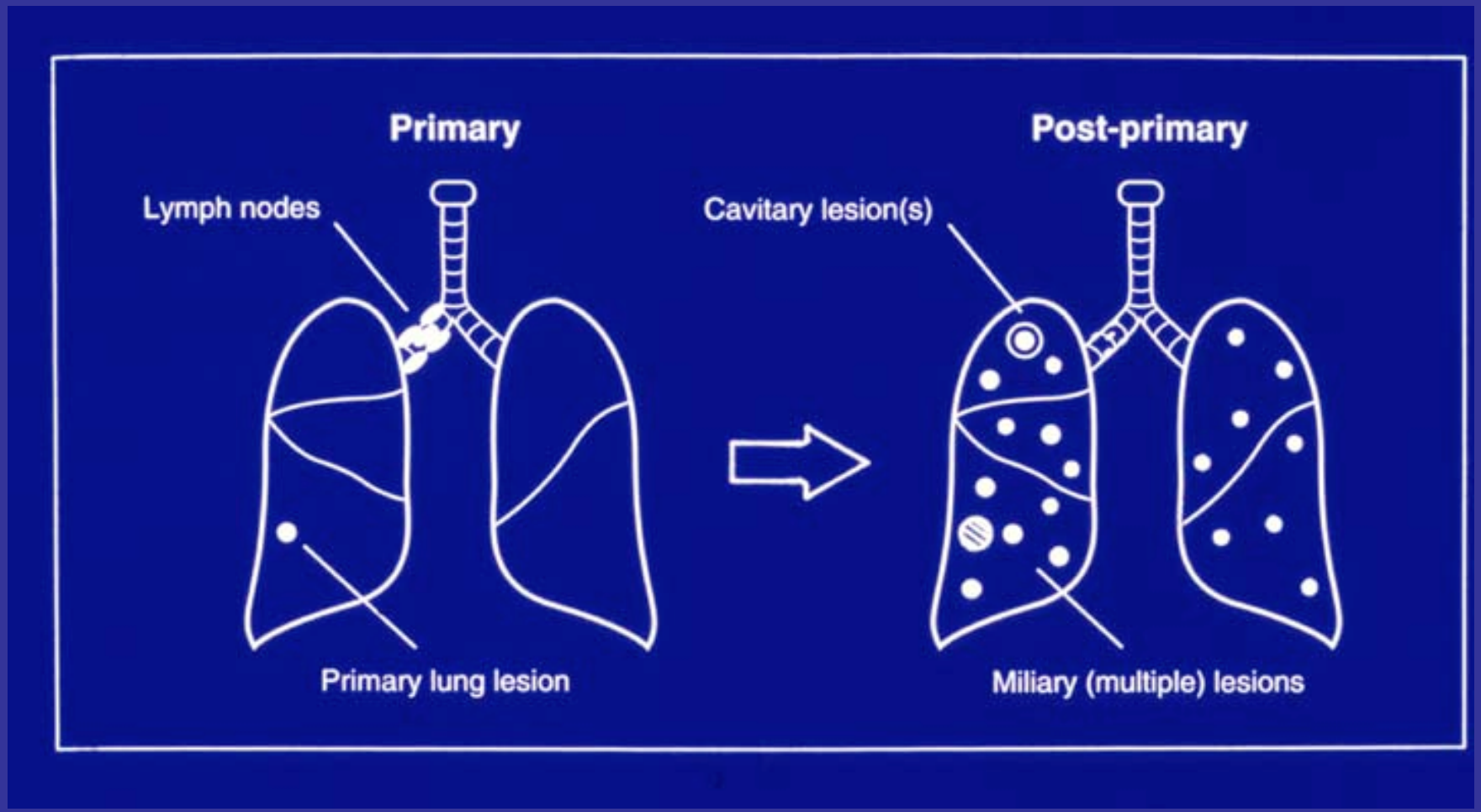
4) No build-up of humidity within the chamber

5) Two HEPA filters in series sterilize the effluent air; certification annually; no replacement neccessary in 20 years!






Lymph nodes
2
1
Primary lung lesion
4
Spleen
3


Primary
Post-primary
Lymph nodes
Cavitary lesion(s)
Primary lung lesion
Miliary (multiple) lesions

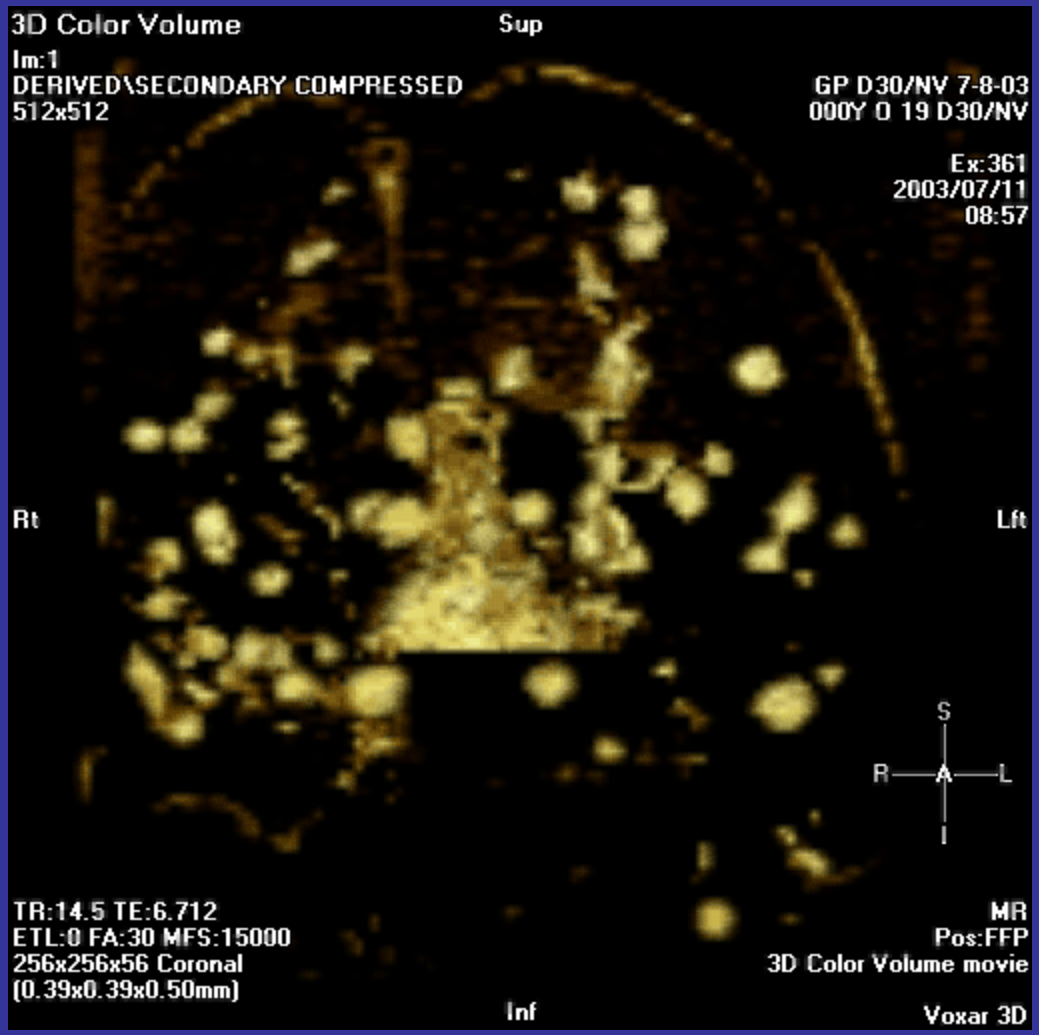

3D Color Volume
Sup
Im:1
DERIVED\SECONDARY COMPRESSED
512x512
GP D30/NV 7-8-03
000Y O 19 D30/NV
Ex:361
2003/07/11
08:57
Rt
Lft
S
R
A
L
I
TR:14.5 TE:6.712
ETL:0 FA:30 MFS:15000
256x256x56 Coronal
(0.39x0.39x0.50mm)
MR
Pos:FFP
3D Color Volume movie
Inf
Voxar 3D

Table 8

Retention of viable *A. fumigatus* spores in the lungs of guinea pigs immediately following aerosol challenge

Exposure Group	Animal Number	Spores Retained in Lung (propagules/gm)[1]	Mean	Log10 of Mean
A1	38	1995	1868	3.27
A2	47	1740		
B1	13	3300	2768	3.44
B2	32	2235		
C1	20	0	0	--
C2	1	0		

[1] Propagules/gm = $\frac{\text{average \# colonies per plate x dilution factor}}{\text{tissue sample weight}}$

Figure 3. Clearance of spores from the lungs of guinea pigs following aerosol challenge with A. fumigatus in the high dose pathogenicity study.

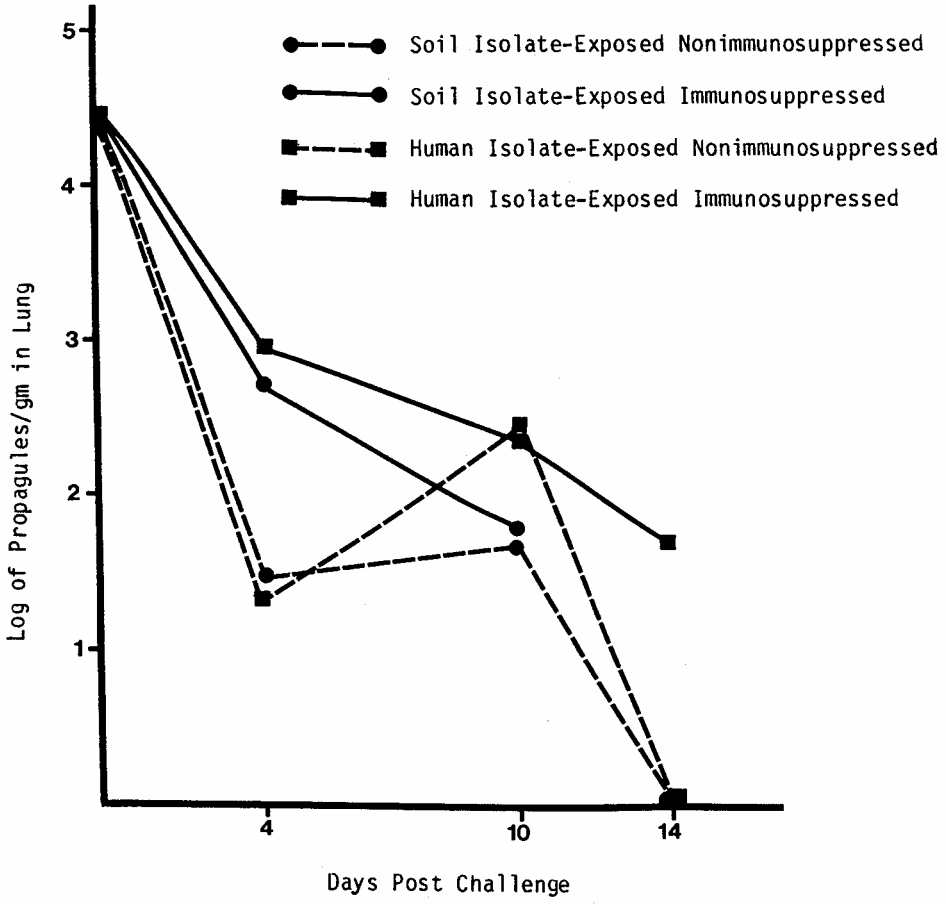


Table 20

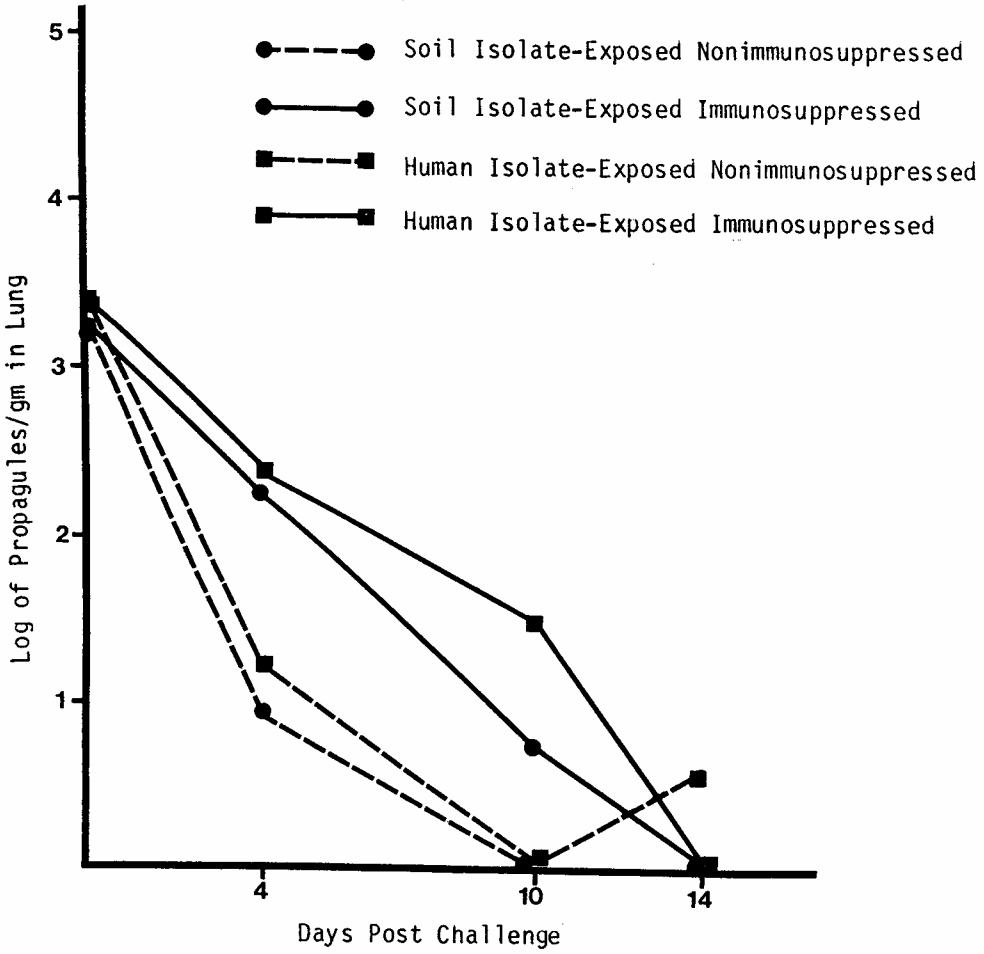
Retention of viable A. fumigatus spores in the lungs of guinea pigs immediately following aerosol challenge in the high dose pathogenicity study[1]

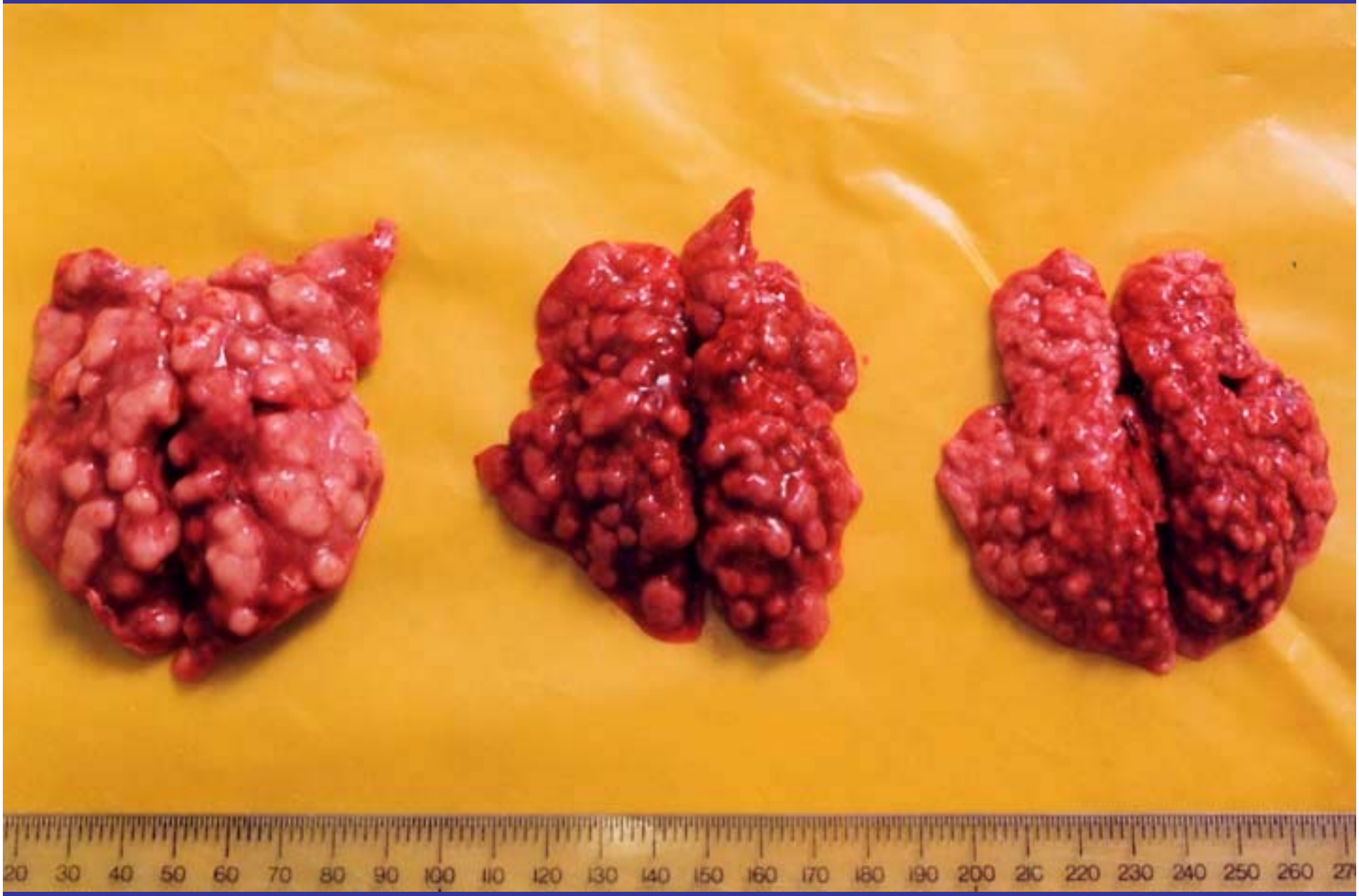
Exposure Group	Animal Number	Spores Retained in Lung (propagules/gm)[2]	Mean	Log of Mean
A1	40	35,150	32,008	4.50
A2	16	28,866		
B1	9	28,860	32,292	4.51
B2	14	35,724		
C1	5	0	0	--
C2	23	0		

[1] A1 and A2 were the soil isolate-exposed groups, B1 and B2 were the human isolate-exposed groups, and C1 and C2 were the saline exposed control groups.

[2] propagules/gm = $\frac{\text{mean colonies per plate x dilution factor}}{\text{organ sample weight}}$

Figure 2. Clearance of spores from the lungs of guinea pigs following aerosol challenge with A. fumigatus in the low dose pathogenicity study.




20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180 190 200 210 220 230 240 250 260

COMPARISON OF 1° AND 2° LUNG LESIONS FROM BCG-VACCINATED AND NON-VACCINATED GUINEA PIGS

CHARACTERISTIC	1° lesion Non-vacc	2° lesion Non-vacc	1° lesion BCG-vacc
Route of implant	Airway	Blood	Airway
CMI present	No	Yes	Yes
Onset of resistance	Delayed	Delayed	Delayed
Granuloma size	Large	Small	Small
Necrosis	Yes	No	No
Max bacillary levels	High	Low	Low

INSTITUTIONAL DECISIONS REGARDING THE USE OF THE MADISON AEROSOL CHAMBER

1) BL-3/4 facilities

2) SOP/personnel training

3) Risk/Benefit analysis

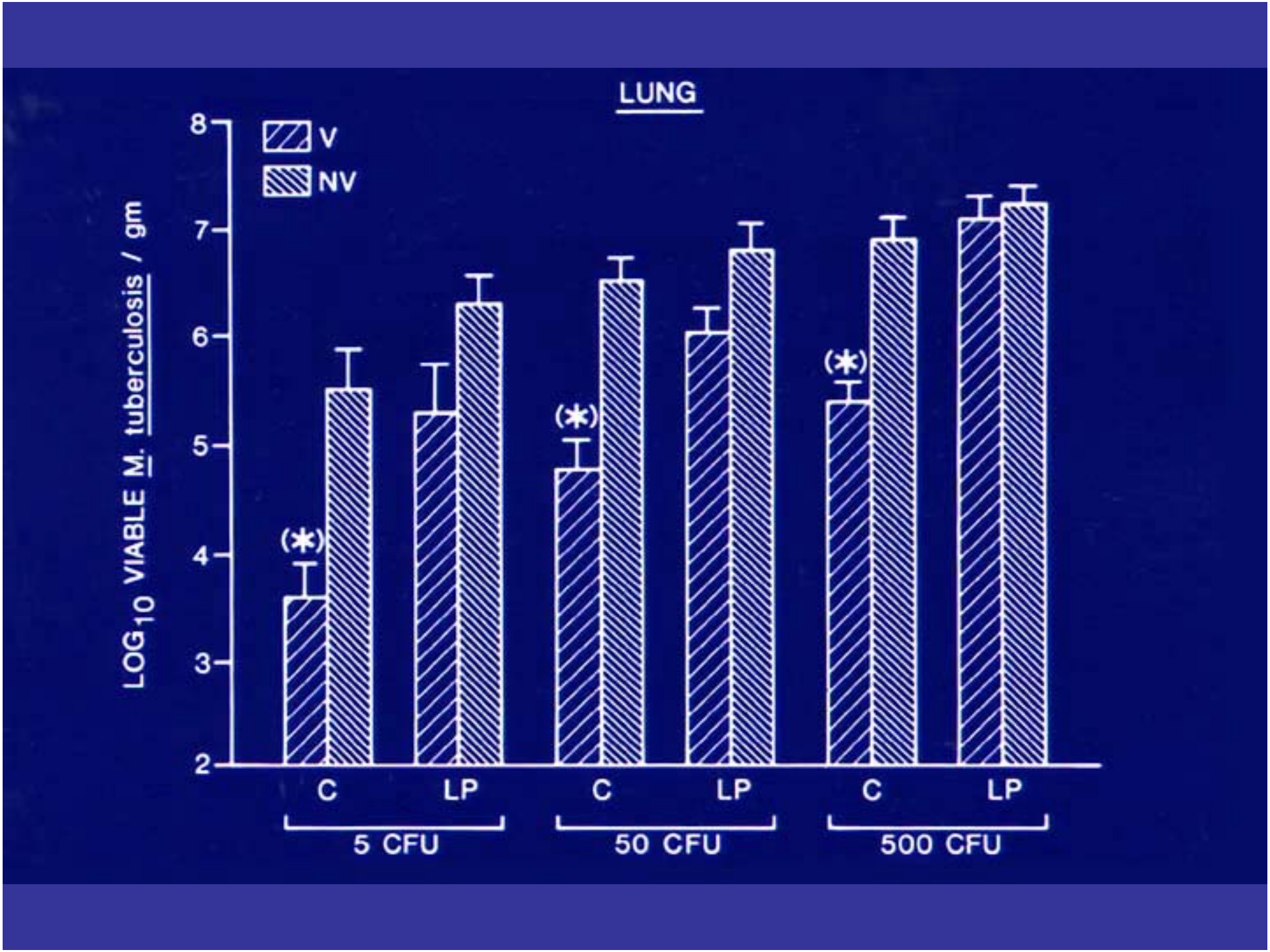
   a. Selfish motives - prestige; indirect costs

   b. Altruistic motives - genuine desire to contribute to the solution of important human health problems

   c. Biological relevance for the study of pulmonary infections

   d. What is the real (as opposed to the perceived) risk?


FAN
TEST
POWER
DEHUMIDIFIER
TEST
END CYCLE


LUNG
V
NV
LOG10 VIABLE M. tuberculosis / gm
8
7
6
5
4
3
2
(*)
(*)
(*)
C
LP
C
LP
C
LP
5 CFU
50 CFU
500 CFU